FIGURE 1: SEQ NO:1

Nucleotide Sequence Tankyrase homologue isotype1

CTTTGAAGACACTGGATTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA
TTAGCTGTGAGCAGATCTTTTTTTGTTGCTTCTTGTAGTCCCCCAGTTTAGCAGAAACATTCTGTGAGA
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA
CATTTGAACTTTGAGCTTTCAGTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAGGTTTTGGGCG
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGCGACATGGTGCAGA
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTGGA
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGTGA
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA
TGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA
ATTCACTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTCTTAAGTTATGG
TGCAGACCCAACACTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAA
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTGCA
TTGTGCTGCTGCATCTCCATATCCCAAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAAA
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA
CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACAT
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGG
TATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAAAC
TGTAAAAAAAACTGTGTACTGTTCAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACT
TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAATATCTGCTACAGCATGGAGCTGATGTGCA
TGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATGGACATTATGAAGTTGCAGA
ACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGC
AGCAGCAAAAGGAAAATATGAAATTTGCAAACTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAAAA
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG
AGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGA
TAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAA
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TTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGA
TTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCCATCTGCTCTGCCCTCTTG
TTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTCTTCAGGTCC
ATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACTTATCTGGGAGTTTTTCAGAACTGTC
TTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAAGGAGGTTCCAGGAGTAGA
TTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGGATATATTTGAGAGAGAACA
GATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG
ACATAGGCACAAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTT
AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA
CAGATACAATATTCTCAAGATTCAGAAGGTTTGTAACAAGAAACTATGGGAAAGATACACTCACCGGAG
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTCATGGGTCTCCTTTTGT
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT
TTATTTTGCTGAAAACTCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCC
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GTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG
GCCCAGTGTAAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAAACTA
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAAAA
AA

FIGURE 2: SEQ ID NO:2

Nucleotide Sequence Tankyrase homologue isotype2

CGCGCTGCTCCGCCCGCCGCGGGGCAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCGTGGGCGCGG
CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCGGGCCCTGAGCGCGTCTTCTC
CGGGGGGCCTCGCCCTCCTGCTCGCGGGGCCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG
TGGCGGCGGCCAGGATCATGTCGGGTCGCCGCTGCGCCGGCGGGGGAGCGGCCTGCGCGAGCGCCGCGG
CCGAGGCCGTGGAGCCGGCCGCCCGAGAGCTGTTCGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA
AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCCGCTGCACT
TCGCCGCAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC
GTGATGATGGGGGCCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC
TTTTGCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA
TTAAAGGAAAGATTGATGTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG
ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG
ATGAACTCTTAGAAAGTGCCAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATG
TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT
TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAA
ATGCAATGGACTTGTGGCAATTCACTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT
CTCTTCTCTTAAGTTATGGTGCAGACCCAACACTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGG
CTCCCACACCACAGTTAAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC
GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAA
CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAAGAAAGCAAATATGTGAACTGT
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTG
AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATC
TTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCT
ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTAC
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAA
AGGCTGGAGATGTCGAAACTGTAAAAAAACTGTGTACTGTTCAGAGTGTCAACTGCAGAGACATTGAAG
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAATATCTGCTAC
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATG
GACATTATGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAAT
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CAGACCCTACCAAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATA
TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA
AGAAGTTGTCTTCTCCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT
TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC
AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC
TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTCACACCTTTGCACGAAGCAGCCC
AAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGG
AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC
CATCTGCTCTGCCCTCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAG
ATGCTCTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACTTATCTG
GGAGTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAA
AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGG
ATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGA
TTGGAATCAATGCTTATGGACATAGGCACAAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAAC
AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG
ATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTC
ATGCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTCAGAAGGTTTGTAACAAGAAACTATGGG
AAAGATACACTCACCGGAGAAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTAT
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GAGGAGGTACTGGGTGTCCAGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT
GCCGGGTAACCTTGGGAAAGTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTC
ATCACTCAGTCACTGGTAGGCCCAGTGTAAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG
AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAA

TAGTTATTTTAAGA[redacted]TAATTCCACTGAACCTAAAATCATCAAAGCAGC[redacted]GGCCTCTACGTTTTAC
TCCTTTGCTGAAAAAAAAAAA

FIGURE 3: SEQ ID NO:3

Amino Acid Sequence Tankyrase homologue isotype1

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFGHAEVVNLLLRHGADPNARDNWNYTPLHEAAIKG
KIDVCIVLLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEK**M**MALLTPLNVNC
HASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTELLVKHGACVNAM
DLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAPTPQLKERLAYEFKGHSLLQAAREA
DVTRIKKHLSLEMVNFKHPQTHETALHCAAASPYPKRKQICELLLRKGANINEKTKEFLTPLHVASEKA
HNDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIISLQGFTALQMGNENVQQL
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG
ADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGKYEICKLLLQHGADP
TKKNRDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA
GYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG
RTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSALPSCYKPQVLNGVRSPGATADAL
SSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMDIF
EREQITLDVLVEMGHKELKEIGINAYGHRHKLIKGVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDK
EFQSVEEEMQSTVREHRDGGHAGGIFNRYNILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHG
SPFVNAIIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFCRV
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSV

Bold = potential starting methionine

FIGURE 4: SEQ ID NO:4

Amino Acid Sequence Tankyrase homologue isotype2

RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV
AAARIMSGRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF
AAGFGRKDVVEYLLQNGANVQARDDGGLIPLHNACSFGHAEVVNLLLRHGADPNARDNWNYTPLHEAAI
KGKIDVCIVLLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTELLVKHGACVN
AMDLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAPTPQLKERLAYEFKGHSLLQAAR
EADVTRIKKHLSLEMVNFKHPQTHETALHCAAASPYPKRKQICELLLRKGANINEKTKEFLTPLHVASE
KAHNDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIISLQGFTALQMGNENVQ
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ
HGADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA
DPTKKNRDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL
AAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ
KGRTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSALPSCYKPQVLNGVRSPGATAD
ALSSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMD
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLIKGVERLISGQQGLNPYLTLNTSGSGTILIDLSPD
DKEFQSVEEEMQSTVREHRDGGHAGGIFNRYNILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLF
HGSPFVNAIIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC
RVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

FIGURE 5

Schematic Presentation of Dominant negative Mutants for Tankyrase Homologue

Dominant Negative Mutants:

Truncation: 429ΔC- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25;18(50):7010-5)
Point mutant: E945AΔC- conserved residue in PARP domain, thought to be important in NAD+ binding

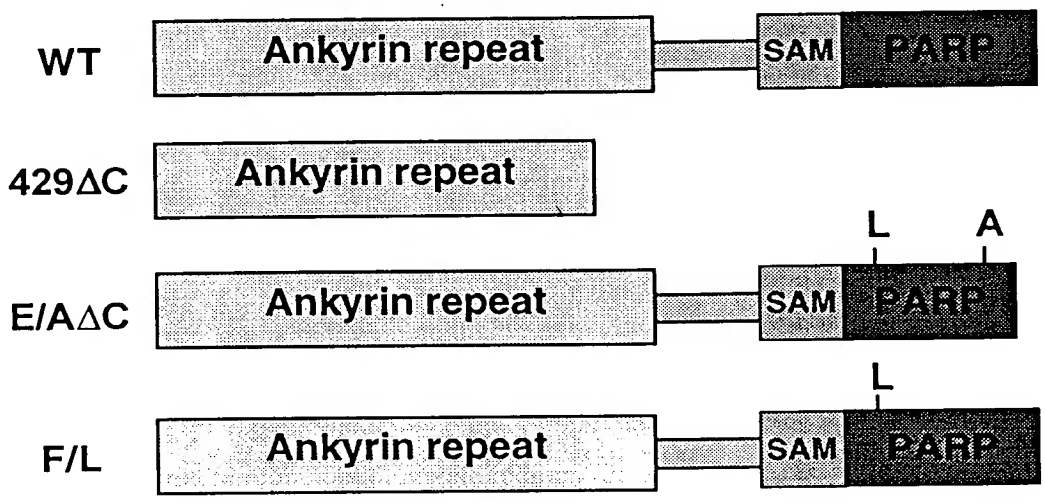


FIGURE 6

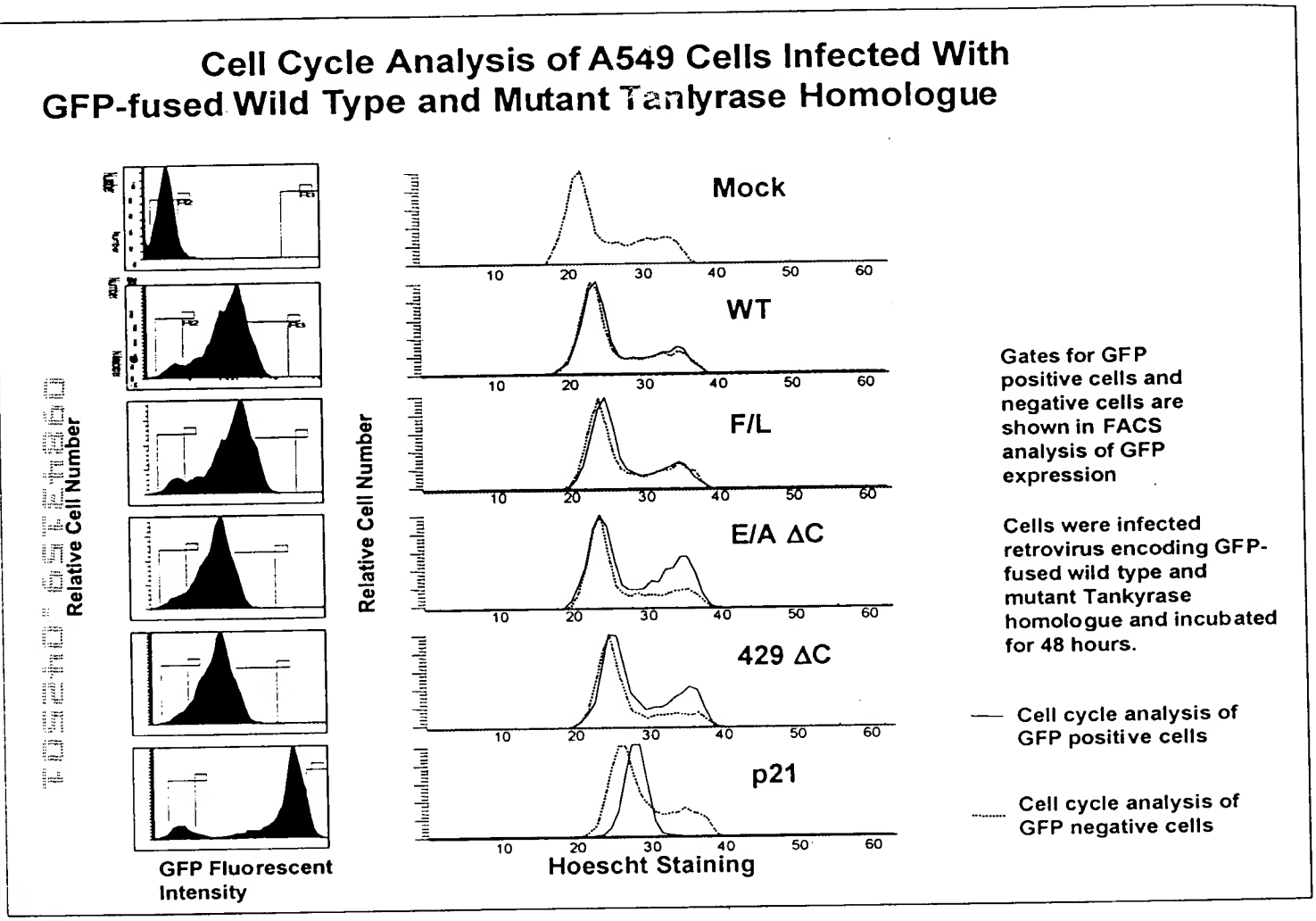

Cell Cycle Analysis of A549 Cells Infected With GFP-fused Wild Type and Mutant Tankyrase Homologue
Relative Cell Number
GFP Fluorescent Intensity
Relative Cell Number
Mock
WT
F/L
E/A ΔC
429 ΔC
p21
10
20
30
40
50
60
Hoescht Staining
Gates for GFP positive cells and negative cells are shown in FACS analysis of GFP expression
Cells were infected retrovirus encoding GFP-fused wild type and mutant Tankyrase homologue and incubated for 48 hours.
Cell cycle analysis of GFP positive cells
Cell cycle analysis of GFP negative cells

FIGURE 7

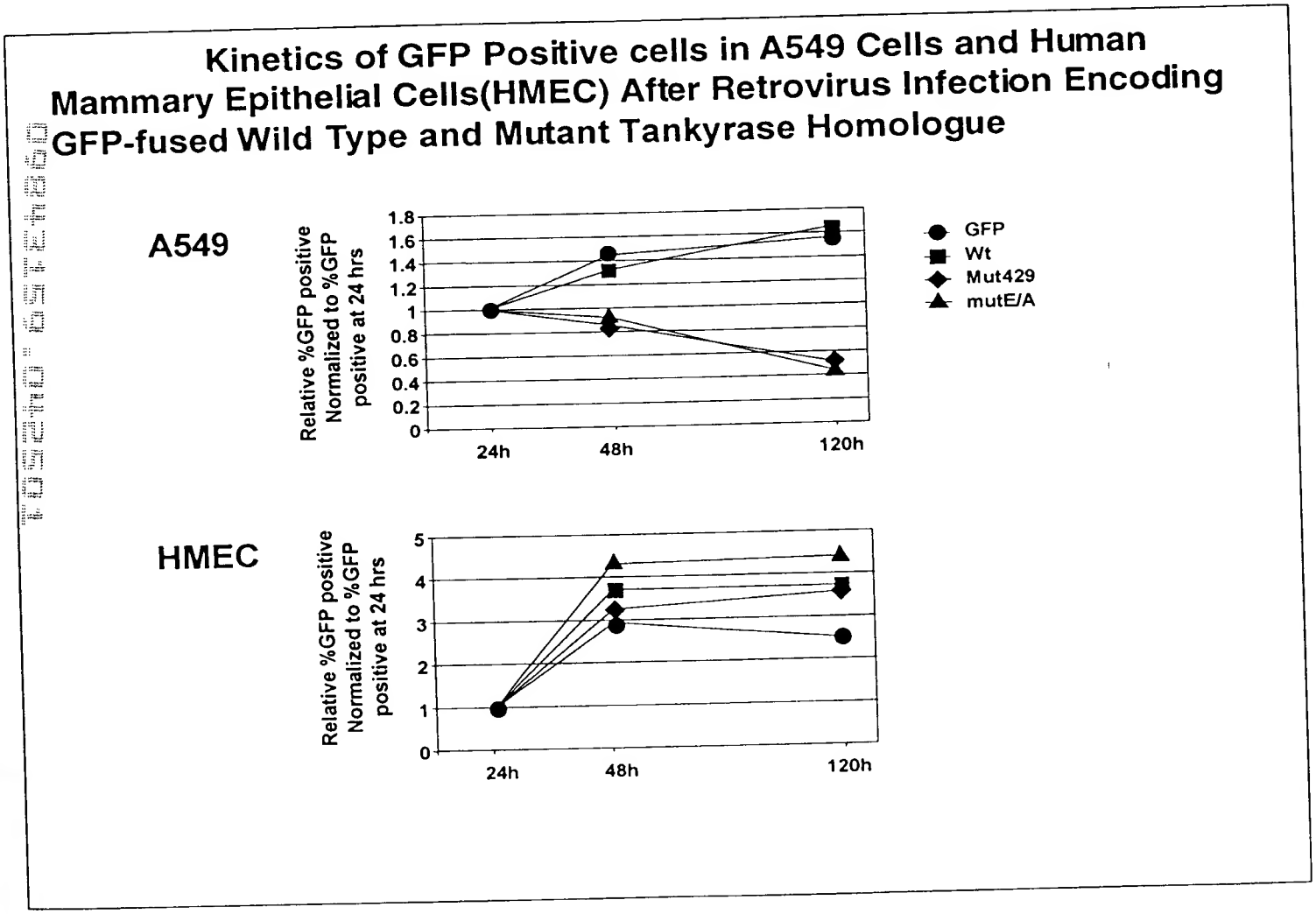
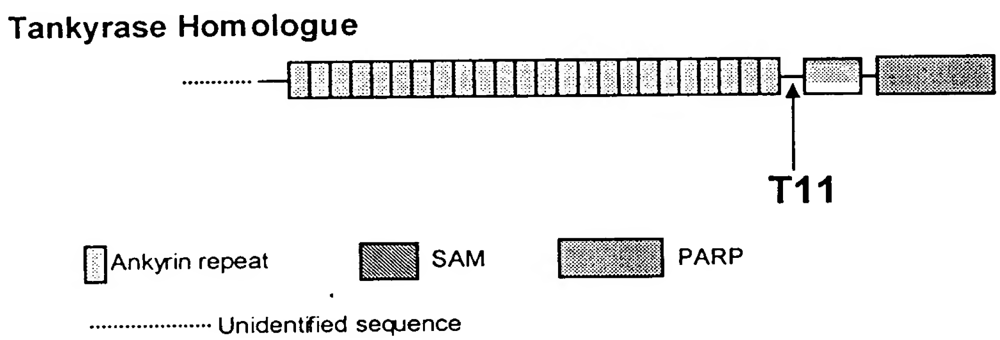

Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells(HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue
A549
Relative %GFP positive Normalized to %GFP positive at 24 hrs
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
24h
48h
120h
GFP
Wt
Mut429
mutE/A
HMEC
Relative %GFP positive Normalized to %GFP positive at 24 hrs
5
4
3
2
1
0
24h
48h
120h

FIGURE 8

The Binding Site of Antisense Oligos Against Tankyrase Homologue



T11

```
                    GTGGAACAGAGGGTGCTTCC
Tankyrase Homologue GTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAAGGAGGTTCCAGGAGTAGATTTTAGCAT 2838
Tankyrase           ATGCAGGGGATGGCGCCGCGGGAACAGAAAGGAAGGAAGGAGAAGTTGCTGGTCTTGACAT 3091
                     ** *   ** ** **  *  *    ** *  ***** *    **  *  * * **  ***
```

FIGURE 9

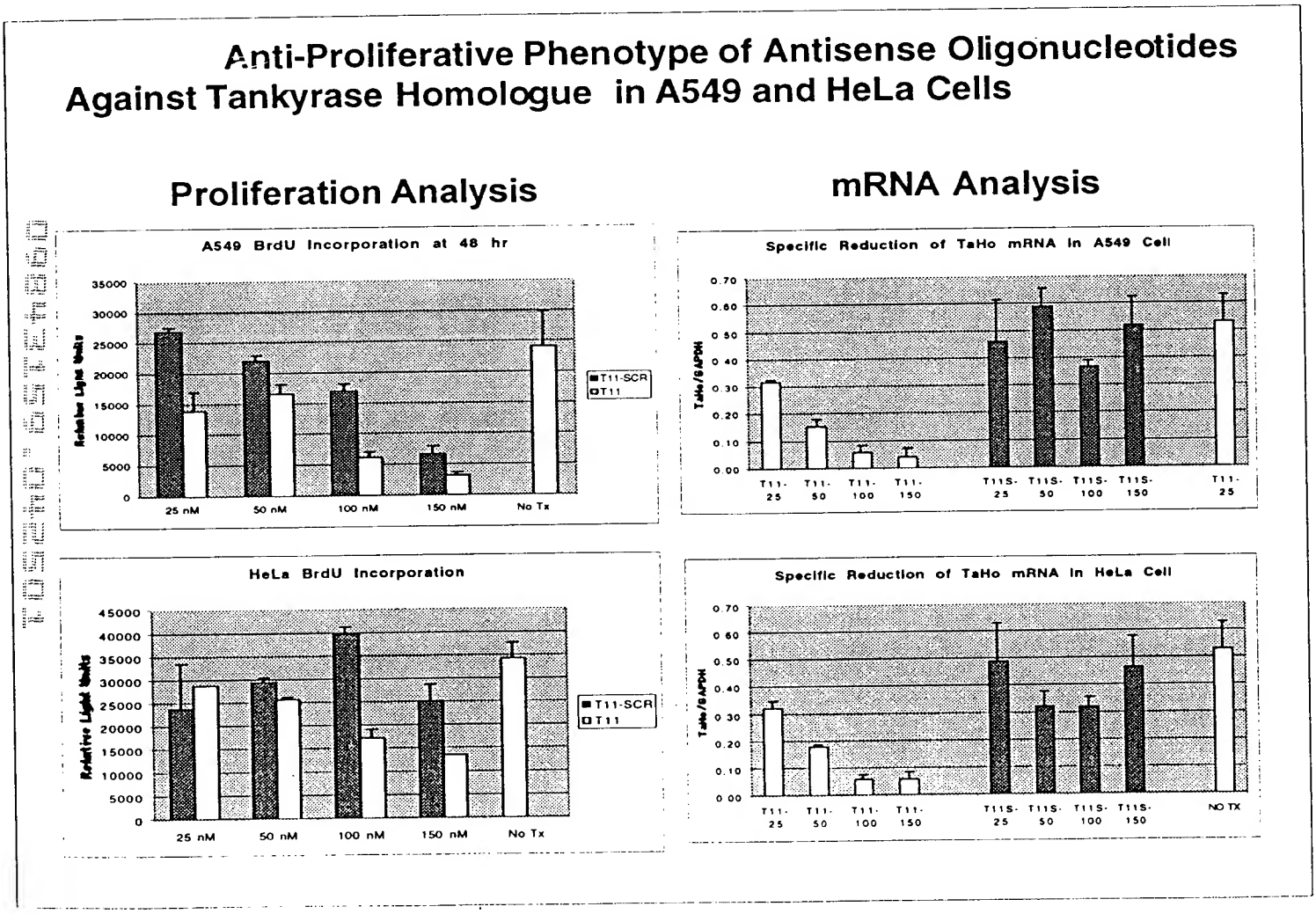

Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells
Proliferation Analysis
mRNA Analysis
A549 BrdU Incorporation at 48 hr
Relative Light Units
35000
30000
25000
20000
15000
10000
5000
0
25 nM
50 nM
100 nM
150 nM
No Tx
T11-SCR
T11
Specific Reduction of TaHo mRNA in A549 Cell
TaHo/GAPDH
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
T11-25
T11-50
T11-100
T11-150
T11S-25
T11S-50
T11S-100
T11S-150
T11-25
HeLa BrdU Incorporation
Relative Light Units
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
25 nM
50 nM
100 nM
150 nM
No Tx
T11-SCR
T11
Specific Reduction of TaHo mRNA in HeLa Cell
TaHo/GAPDH
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
T11-25
T11-50
T11-100
T11-150
T11S-25
T11S-50
T11S-100
T11S-150
NO TX

FIGURE 10

Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and control oligonucleotides (T11S) were transfected with FITC-labeled random 20mer oligonucleotides(FITC), After 48 hours, entire population(R1) and top 5 % (R2)of FITC transfected cells were analyzed for cell cycle.

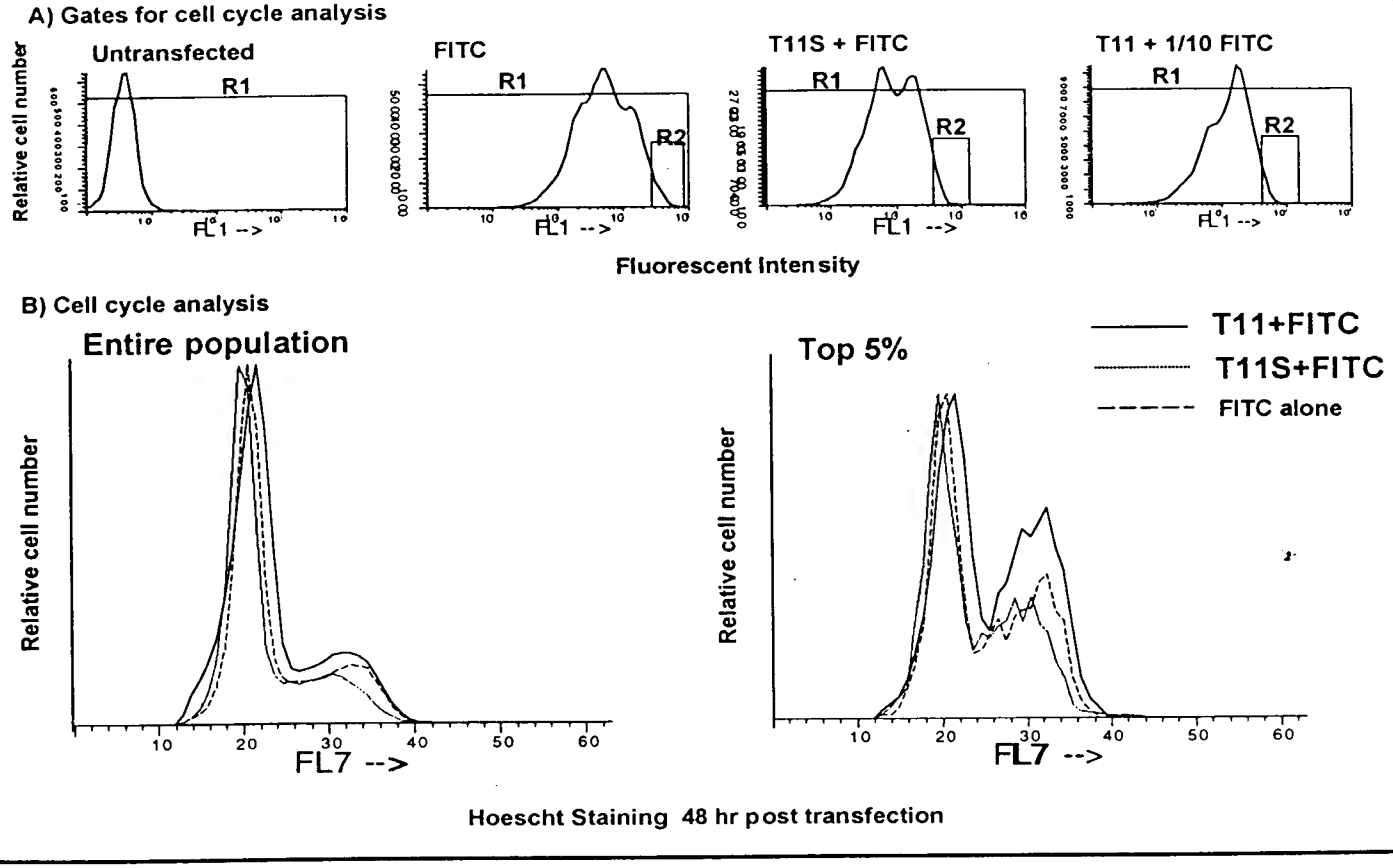


FIGURE 11

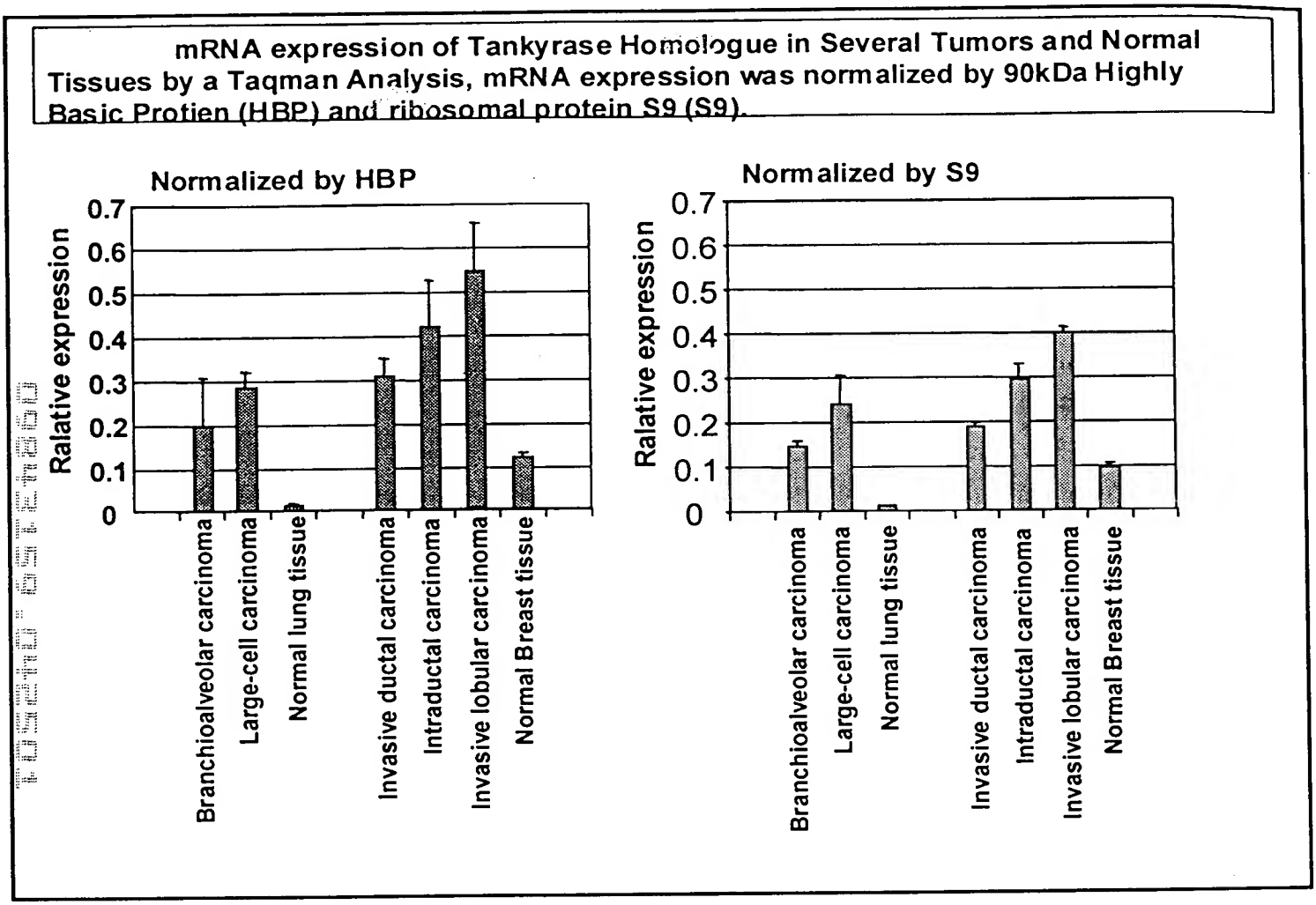

mRNA expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA expression was normalized by 90kDa Highly Basic Protien (HBP) and ribosomal protein S9 (S9).
Normalized by HBP
Ralative expression
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Branchioalveolar carcinoma
Large-cell carcinoma
Normal lung tissue
Invasive ductal carcinoma
Intraductal carcinoma
Invasive lobular carcinoma
Normal Breast tissue
Normalized by S9
Ralative expression
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Branchioalveolar carcinoma
Large-cell carcinoma
Normal lung tissue
Invasive ductal carcinoma
Intraductal carcinoma
Invasive lobular carcinoma
Normal Breast tissue

FIGURE 12

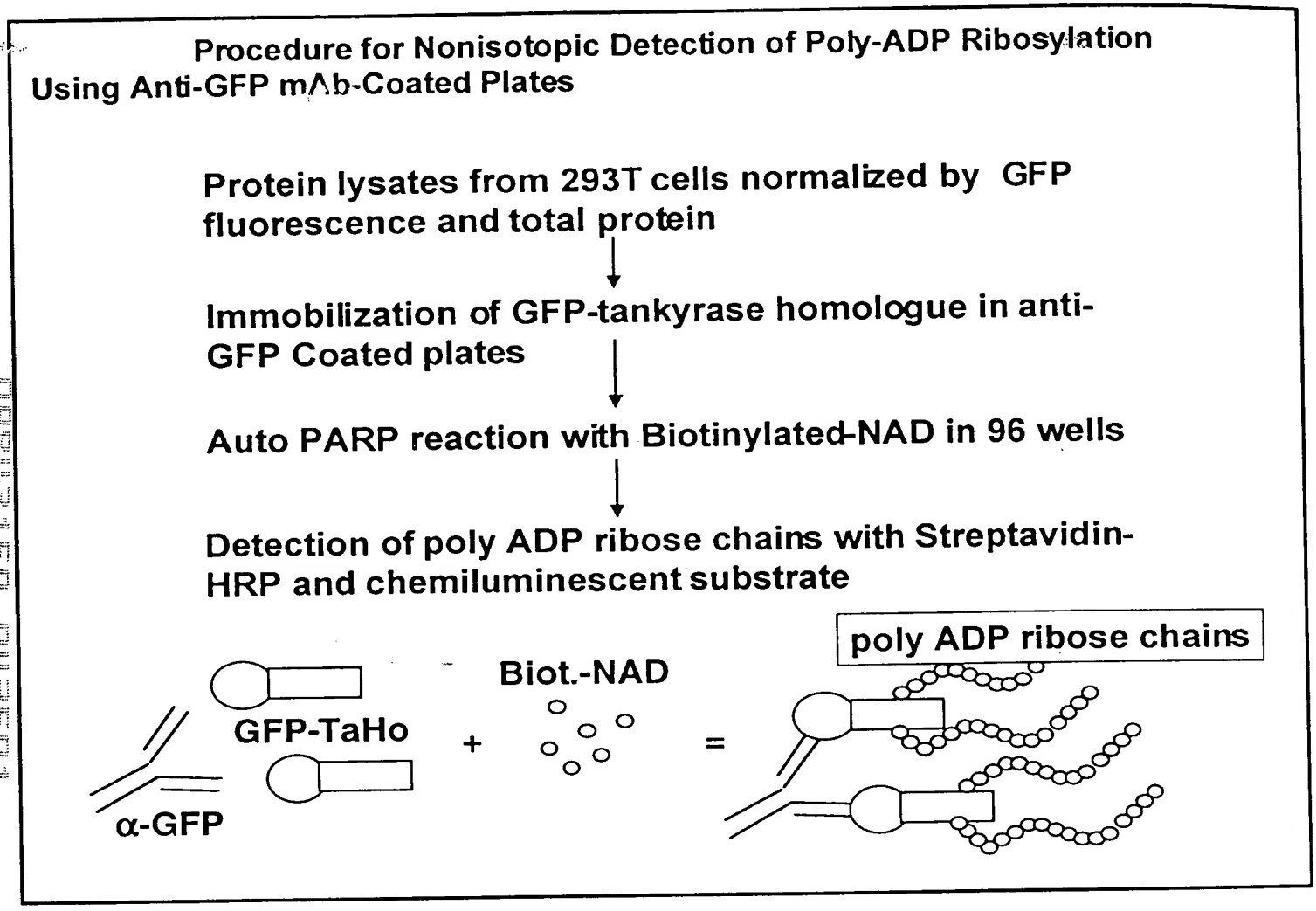

Procedure for Nonisotopic Detection of Poly-ADP Ribosylation Using Anti-GFP mAb-Coated Plates
Protein lysates from 293T cells normalized by GFP fluorescence and total protein
Immobilization of GFP-tankyrase homologue in anti-GFP Coated plates
Auto PARP reaction with Biotinylated-NAD in 96 wells
Detection of poly ADP ribose chains with Streptavidin-HRP and chemiluminescent substrate
poly ADP ribose chains
Biot.-NAD
GFP-TaHo
α-GFP
+
=

FIGURE 13

Non-Isotopic Plate-Based Detection of Taho PARP Activity in the Presence of Biotinylated NAD.

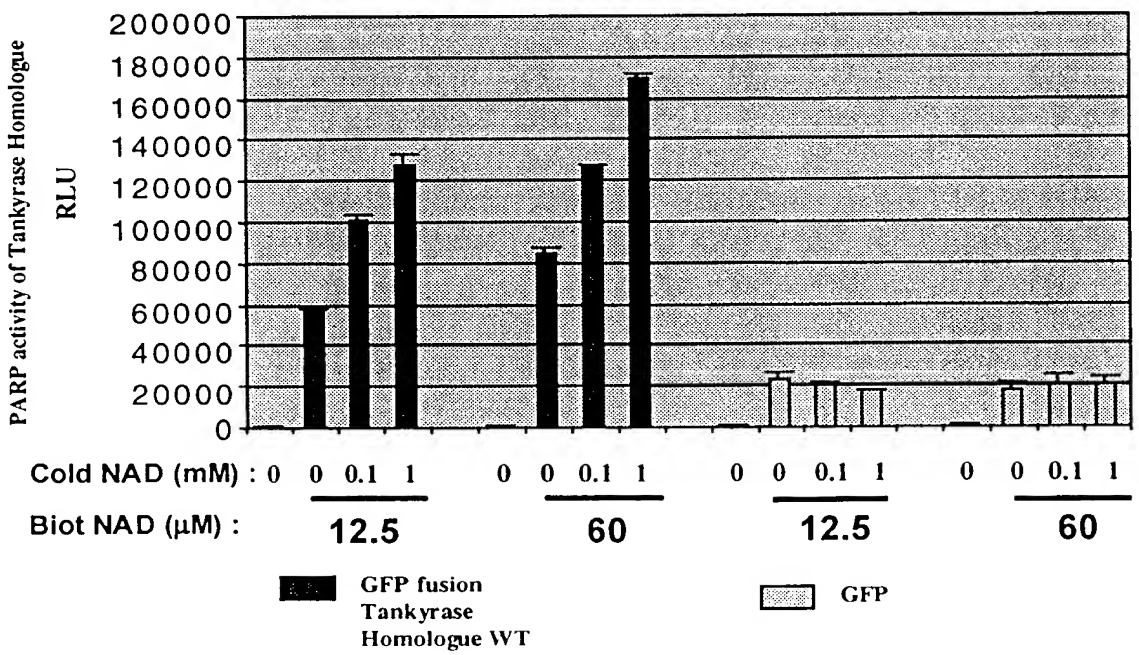


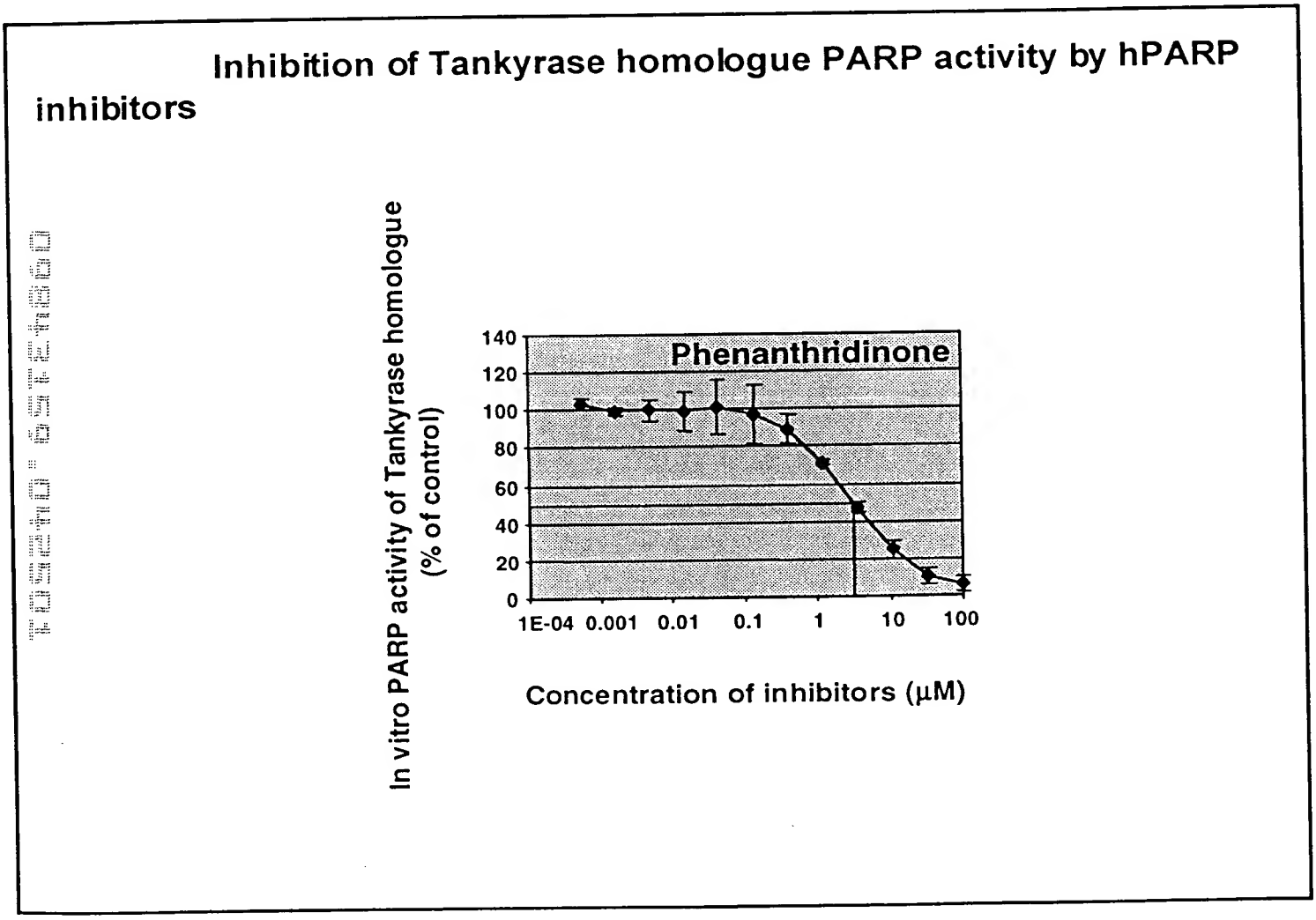
FIGURE 14

Comparison of IC_{50} Values of the PARP Inhibitors

	Approximate IC_{50} (nM)	hPARP assay IC_{50} (nM)		
	TaHo	Rigel	Decker *	Rankin *
3AB	> 50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	> 50 000	30 000	>>5 000	31 000

* *Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172.*
* *Rankin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317.*

FIGURE 15


Inhibition of Tankyrase homologue PARP activity by hPARP inhibitors
In vitro PARP activity of Tankyrase homologue (% of control)
Phenanthridinone
140
120
100
80
60
40
20
0
1E-04
0.001
0.01
0.1
1
10
100
Concentration of inhibitors (µM)

TH-1: Tankyrase homologue isoform-1, TH-2: Tankyrase homologue isoform-2
M (Red): the first methionine in the sequence, Z: stop codon
In this figure, the first methyonine in TH-1 sequence is position 1 (M1)

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Taho F/L mutant has the mutation at position 871

Taho E/A dC mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

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TH-1            ------------------------------------------------------------
TH-2                                  RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQ -231

TH-1            ------------------------------------------------------------
TH-2            AARALSASSPGGLALLLAGPGLLLRLLALLLAVAAARIMSGRRCAGGGAACASAAAEAVE -171

TH-1            -------------------------------------------*GFGRKDVVEYLLQNGA -111
TH-2            PAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHFAAGFGRKDVVEYLLQNGA -111
                         Ankyrin repeat                  Ankyrin repeat

TH-1            SVQARDDGGLIPLHNACSFGHAEVVNLLLRHGADPNARDNWNYTPLHEAAIKGKIDVCIV -51
TH-2            NVQARDDGGLIPLHNACSFGHAEVVNLLLRHGADPNARDNWNYTPLHEAAIKGKIDVCIV -51
                      Ankyrin repeat                  Ankyrin repeat
                                                        •TH1 start
TH-1            LLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV 10
TH-2            LLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV 10
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FIGURE 16 (sheet 1 of 3)

FIGURE 16
(sheet 2 of 3)

FIGURE 16
(sheet 3 of 3)

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TH-1   LHLAAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATD 550
           Ankyrin repeat                   Ankyrin repeat

TH-1   KWAFTPLHEAAQKGRTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSA 610
            Ankyrin repeat                      Ankyrin repeat

TH-1   LPSCYKPQVLNGVRSPGATADALSSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEG 670
                                     Ankyrin repeat

TH-1   ASSLEKKE--VPGVDFSITQFVRNLGLEHLMDIFEREQITLDVLVEMGHKELKEIGINAY 730
                  SAM domain

TH-1   GHRHKLIKGVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDKEFQSVEEEMQSTVREHR 790

TH-1   DGGHAGGIFNRYNILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNAII 850

TH-1   HKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFCR 910
                   • F→L mutation
                   PARP domain

                                     --------A---------LSZ
TH-1   VTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRP 970
                                          •E→A        •Deletion.

TH-1   EGMVDG 976
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